

## Mepolizumab

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### Approved indication: asthma

**Nucala (GlaxoSmithKline)**

**vials containing 144 mg powder for reconstitution**  
**Australian Medicines Handbook section 19.1.6**

Some patients with asthma have severe disease that is not well controlled by inhaled treatments. They may require regular oral corticosteroids to control airway inflammation. In some patients there can be high concentrations of IgE which may respond to treatment with omalizumab. Other patients have high concentrations of eosinophils so these cells are potential targets for new drugs such as mepolizumab.

The life cycle of eosinophils is controlled by interleukin 5. This cytokine may be overproduced in patients with eosinophilic asthma. Mepolizumab is a humanised monoclonal antibody that binds to interleukin 5. This prevents interleukin 5 from binding to its receptors on the surface of eosinophils. A dose of mepolizumab will reduce eosinophils by at least 50%.

As mepolizumab is an immunoglobulin (IgG) it has to be given by injection. When reconstituted with water for injection, the powder forms a solution with a strength of 100 mg/mL. The usual dose is 100 mg injected subcutaneously every four weeks. After injection into the arm the bioavailability is 74–80%. The peak concentration is reached in 4–8 days and the terminal half-life following metabolism is 16–22 days. There have been no formal studies of hepatic or renal impairment or of drug interactions.

The Cochrane Airways Group has reviewed eight trials comparing mepolizumab with placebo in 1707 patients. Due to the heterogeneity of the studies the role of mepolizumab was uncertain, but it did reduce exacerbations and improve health-related quality of life in patients with severe eosinophilic asthma.<sup>1</sup>

One of the studies in the review randomised 621 patients with eosinophilic inflammation to intravenous infusions of placebo or mepolizumab 75 mg, 250 mg or 750 mg. Thirteen infusions were given at four-week intervals. Mepolizumab significantly reduced the numbers of eosinophils in the blood. There were 806 asthma exacerbations which required treatment with oral steroids. Compared to placebo the number of exacerbations per patient per year was reduced significantly by all doses of mepolizumab. For example, there was a 48% reduction with the 75 mg dose.<sup>2</sup>

A subcutaneous regimen was included in a trial involving patients with severe eosinophilic asthma who had experienced at least two exacerbations of asthma in the previous year. Treatment was given every four weeks for 32 weeks. There were 449 exacerbations. In the 194 patients assigned to receive mepolizumab 100 mg subcutaneously, the annual exacerbation rate was 0.83 compared with 1.74 in the 191 patients assigned to placebo.<sup>3</sup>

Another trial assessed whether subcutaneous mepolizumab can reduce the amount of oral corticosteroids consumed by patients with severe eosinophilic asthma. The 135 patients in the trial had been taking 5–35 mg of prednisone or equivalent for at least six months. After injecting mepolizumab or a placebo every four weeks for 20 weeks their use of corticosteroids was reassessed. The median reduction from their baseline dose was 50% for the patients taking mepolizumab. There was no reduction in the placebo group. The annual exacerbation rate was 1.44 with mepolizumab and 2.12 with placebo.<sup>4</sup>

Safety information is available for 1018 patients who took mepolizumab 100 mg subcutaneously. Common adverse events were headache and nasopharyngitis. Injecting an antibody can cause hypersensitivity reactions which may have a delayed onset. Approximately 6% of patients developed antibodies against mepolizumab. Injection site reactions affected 8% versus 3% of the placebo group. As eosinophils have a role in the immune response, mepolizumab may alter the response to parasitic infections. Although there were only a few cases of herpes zoster, two of them were serious. There is currently no information about the drug's safety in pregnancy, lactation or in children younger than 12 years.

The optimum use of mepolizumab is yet to be determined. Not all patients benefit, for example 36% were unable to reduce their dose of oral corticosteroid, withdrew from treatment or had a lack of asthma control.<sup>4</sup> Some of the patients suitable for treatment with mepolizumab may also qualify for treatment with omalizumab so the treatments should be compared. If a patient with severe refractory eosinophilic asthma is prescribed mepolizumab, how long should they take it for? A follow-up of some of the patients in the trials found that after stopping treatment there was a rise in eosinophil count and an increase in asthma symptoms and exacerbations.<sup>5</sup>

**T T** manufacturer provided additional useful information

### REFERENCES

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## NEW DRUGS

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the European Medicines Agency and the Therapeutic Goods Administration.